REVIEW ARTICLE

Post orgasmic illness syndrome: a review

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POIS is a rare condition characterized by multisystem symptoms with unclear aetiology. Various attempts have been made to characterize this condition and knowledge is still evolving regarding its aetiology and effective treatment. We have summarized the findings in the English language literature for this rare condition. PubMed search was performed and over 300 English language articles which were screened for relevance. 34 articles were deemed suitable for inclusion. POIS occurs in age range of 21–61 years. Onset of symptoms is usually within 45 min and lasts for an average of 7 days. Primary POIS accounts for approximately half of the cases in literature. The three commonest symptoms were fatigue (68.7), poor concentration (63.9%) and irritation (51.9%). Treatments with variable efficacy which have been proposed include hyposensitisation, antihistamines, alpha blockers, NSAIDS and testosterone replacements. POIS is an important condition which affects the quality of life of men. It is vital that it is managed on a sound scientific basis

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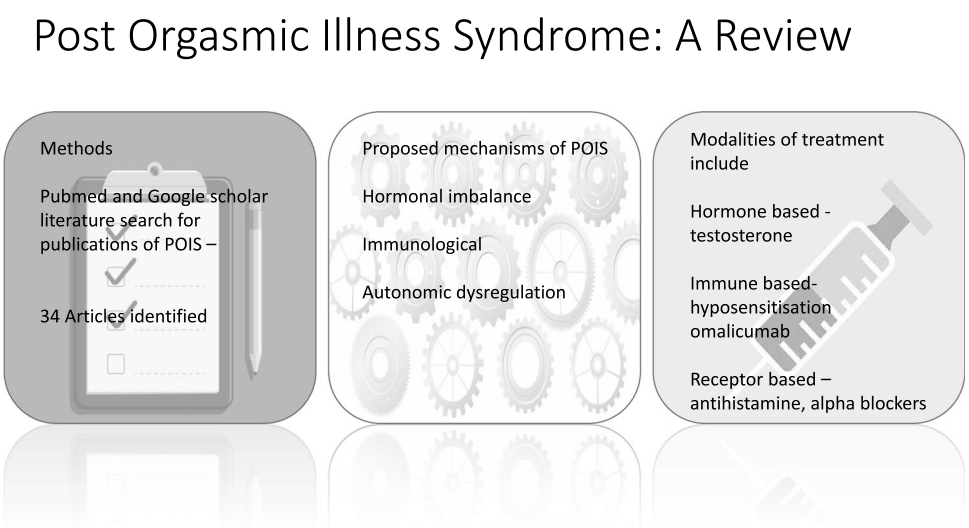
Graphical Abstract



INTRODUCTION

Post orgasmic illness syndrome, (POIS) is a rare condition first described by Waldinger and Schweitzer in 2002 [1]. Since then, although an increasing body of evidence has emerged resulting in clearly defined criteria for diagnosis, there remains a paucity of high-quality studies assessing effective therapy. In addition, the exact pathophysiology remains unclear and remains the subject of much debate. The epidemiology of POIS is unknown, with no specific geographical or racial clustering of cases and the age range within the reported cases is 21–61 years [2, 3]. To date, over 465 cases have been reported in English language publications.

Symptoms such as extreme fatigue, nasal congestion and itchy eyes can occur with masturbation, intercourse or spontaneous nocturnal ejaculation and may start within a few seconds with symptoms sometimes lasting days after ejaculation [1].

The aim of this review is to summarize our current understanding and knowledge of this disease.

MATERIAL AND METHODS

PubMed was used to search for English language articles from 2002 to 2023 using the terms: post orgasmic illness, post orgasmic illness syndrome, post orgasmic syndrome, POIS, post orgasmic lethargy. This was complemented by search of Google search engine for relevant articles.

In total, 332 publications were identified.

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Article selection included studies of any design on POIS in men and publication in a peer-reviewed journal. Manuscripts were then manually screened for relevance with a total of 34 papers being deemed suitable for inclusion.

Data from selected articles were tabulated with Excel spreadsheet (Microsoft Office 365) and statistical analysis for frequency, median and interquartile range were computed.

RESULTS

34 articles were reviewed after screening the initial 332 publications obtained from the search, (Table 1).

DISCUSSION

Symptoms/Diagnosis

POIS presents with a cluster of symptoms (Table 2), with onset typically occurring within 45 min of ejaculation (Table 3) and usually resolving spontaneously within 7 days [2, 4–9].

POIS is classified into primary and secondary. While primary POIS occurs with the first ejaculation during puberty, secondary POIS occurs later in life after a period of symptom free ejaculation.

Primary POIS has been reported in approximately 46% of all cases in the literature, similar to an early case series by Waldinger et al. [9] who reported 49% of patients experienced onset at puberty, whilst a later series by Reisman et al. [10] found that only 14% of patients suffered from primary POIS.

There are important associations with POIS such as premature ejaculation and allergy. In 2011, Waldinger et al. [9] reported one of the largest case series with 45 patients with POIS. More than half of these men reported premature ejaculation with documented intravaginal ejaculatory latency time of less than 1 min. This finding has been supported by other studies [2, 11]. A similar percentage of 58% has a history of atopy with many of these men suffering from hay fever, allergy to animal dander or dust mite [9].

Waldinger originally proposed five diagnostic criteria, (Table 4) and seven symptom cluster domains, (Table 5) which help to identify patients with POIS, however they have not yet been proven to impact treatment or prognosis [9].

There are seven clusters of symptoms expressed in the own words of the patient according to Waldinger et al. [9].

Attempts have been made to validate these criteria in a recent study of over 100 men which showed that 97% of men with a diagnosis of POIS fulfilled three or more diagnostic symptom criteria with 39% fulfilling all 5.

44% of these patients did not always have symptoms with every episode of ejaculation, thus a proposal was made to amend criterion number 3 (symptom present in greater than 90% of ejaculation episodes). The drawback of this study is that only 20% have received a formal diagnosis from their health care provider and information was collected through online forums [12]. A similar online study identified POIS in 302 patients of which only 51% had sought medical opinion [13]. If the contribution of these studies [12, 13] are considered, there are over 465 cases of POIS in literature.

Pathophysiology

There are several theories relating to the aetiology of POIS, (Table 6) [2, 7, 9, 11, 14, 15]

Several studies have proposed an immunological basis for POIS [2, 6, 9], with the dominant theory pointing to a spectrum of hypersensitivity reaction to seminal fluid Table 7. While the sudden onset nature of POIS would support a type 1 hypersensitivity syndrome, the delayed onset of flu-like illness is more in keeping with a type IV reaction. Positive skin prick testing, an example of type IV hypersensitivity, has been demonstrated in many studies [4, 9, 16], with a reactive wheal greater than 5 mm in response to an intradermal injection of 1 in 40,000 dilution autologous semen accepted as a positive test [4].

Although Waldinger et al. [9] were able to elicit positive skin prick test in 88% with diluted autologous semen, they were unable to demonstrate elevated levels of IgE in these subjects, in keeping with several other studies [2, 6, 8, 10].

Conversely, utilizing sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS PAGE), Western blotting and ELISA, Kim et al. were able to demonstrate serum semen-specific IgE in a Korean patient and this remains an area of continued focus and research [16].

Jiang et al. [2] demonstrated positive skin prick test in patients with and without a diagnosis of POIS leading to the concept of an opioid withdrawal mechanism for POIS consisting of endogenous opioids depletion during ejaculation.

In contrast, others [8] have been unable to demonstrate a positive skin test in subjects, despite using advanced techniques such as immunoblotting and western blot, suggesting a possible neurobiological aetiology.

An autoimmune mechanism has been proposed whereby antigen-presenting cells in the urethra recognize peptides from semen thus stimulating T-cell activation [9].

Waldinger et al. described this syndrome in women postulating the antigen to be female prostatic tissue located around the upper vagina. In males, the antigen responsible is a component of seminal fluid not spermatozoa. The persistence of symptoms in 3 men who have had vasectomy supports this theory [17].

Autonomic dysregulation has been suggested by some, suggesting dysregulation of the sympathetic nervous system with some benefit being realised with alpha blockade therapy. The response rate is in the range of 57 to 100% [10, 18].

Table 1. Article types reviewed [1–14, 16–35].

Article type	Number
Review article 17, 25–31	8
Case reports 2–8, 14, 16, 18–24	16
Case series 1, 9–11, 32–34	7
Cross sectional 12, 13, 35	3

Table 2. Summarizes the incidence of symptoms of POIS [1–11, 14, 16, 18–20, 22–24, 32–34].

Symptoms	Percentage
Fatigue	68.7
Fever	50.4
Nasal congestion	37.8
Itchy eyes	33.5
Myalgia	35.8
Poor concentration	63.9
Irritation	51.9
Headache	44.2
Throat symptoms	16.8
Rash	2.4

Table 3. Demonstrates the chronology of POIS symptoms [1–11, 14, 16, 18–20, 22–24, 32–34].

	Median +/−IQR*	range
Time of onset(mins)	45 +/−180	5–4320
Duration of symptoms(days)	7 +/−4.5	2–14

*IQR -Interquartile range.

Table 4. Waldingers diagnostic criteria [9].

Criteria	Description
Criterion 1	One or more of the following symptoms:
	Sensation of a flu-like state, extreme fatigue or exhaustion, weakness of musculature, experiences of feverishness or perspiration, mood disturbances and irritability, memory difficulties, concentration problems, incoherent speech, nasal congestion or watery nose, and itchy eyes
Criterion 2	All symptoms occur immediately (within a few seconds), soon (within a few minutes), or within a few hours after ejaculation that is initiated by coitus or masturbation or spontaneously (e.g., during sleep)
Criterion 3	Symptoms occur always or nearly always (> 90% of ejaculation events)
Criterion 4	Most of these symptoms last for approximately 2–7 days
Criterion 5	The symptoms disappear spontaneously

Table 5. Seven clusters of Waldinger's Diagnostic Criterion 1 Table 5 [9].

Cluster 1 (general cluster)	extreme fatigue, exhausted, palpitations, problems finding words, incoherent speech, dysarthria, concentration difficulties, quickly irritated, can not stand noise, photophobia, depressed mood
Cluster 2 (flu-like cluster)	feverish, extreme warmth, perspiration, shivery, ill with flu, feeling sick, feeling cold
Cluster 3 (head cluster)	headache, foggy feeling in the head, heavy feeling in the head;
Cluster 4 (eyes cluster)	burning, red injected eyes, blurred vision, watery, irritating, itching eyes, painful eyes
Cluster 5 (nose cluster)	congestion nose, watery, runny nose, sneezing;
Cluster 6 (throat cluster)	dirty taste in mouth, dry mouth, sore throat, tickling cough, hoarse voice
Cluster 7 (muscle cluster)	muscle tension in back or neck, muscle weakness, pain muscles, heavy legs, stiffness muscles

Table 6. Potential pathophysiology theories for POIS [1, 2, 7–11, 14].

Immunological
Aberrant cytokine activity
Neuroendocrine
Opioid withdrawal
Autonomic dysregulation
Hormone imbalance – testosterone

Table 7. POIS treatment success rates [4, 6, 7, 9–11, 14, 16, 19, 20, 24].

Treatment	Success rate
Hyposensitisation	60–90%
antihistamines	90%
Alpha blockers	57–100%
NSAID**	80%
Testosterone/ hCG*	50–100%

**hCG* Human chorionic gonadotrophin.
***NSAID* Non- Steroidal anti-inflammatory drugs.

Hormonal imbalance could also be a mechanism of POIS. Some authors report resolution of the symptoms in hypogonadal men with the administration of testosterone or human chorionic gonadotrophin. These occurred in isolated case reports with a response rate of 50- 100% in 3 patients [3, 7, 14]. Dexter et al. reported a case where progesterone administration also led to resolution of symptoms, although this remains an isolated report [15].

Management

Several treatment options have been tried for this rare condition including antihistamines [4], selective serotonin re-uptake inhibitors [7], hormonal manipulation [14], alpha-blockers [10] and hyposensitisation [19].

Using antihistamines to treat POIS has been successful in some studies [4, 20]. Fexofenadine (180 mg daily) is favoured by some because it is long acting, non-sedating and well tolerated, with a reported 90% decrease in symptoms [20].

Recently, a novel approach is the use of flibanserin, a serotonin receptor modulator to manage POIS. This was used in combination with gabapentin [21].

Alpha blockers have been successfully used by various authors [10, 18], with Reisman et al. reporting symptomatic improvement in 57% of patients with POIS with silodosin [10]. The proposed mechanism is anejaculation, but an alternative postulated explanation is control of a dysregulated autonomic nervous system.

Treatment of concomitant testosterone deficiency has been shown to be effective in some studies [3, 7, 14]. Testosterone supplementation in hypogonadal men have also been described although this was used with simultaneous antihistamines and SSRI administration [7]. Similarly, Bolanos et al. reported treating hypogonadal men with human chorionic gonadotrophin with resolution of symptoms after normalization of serum testosterone [14].

The administration of NSAIDs has also been described with the mechanism of action believed to be cytokine blockade [3, 11]. A success rate of up to 80% has been reported with the administration of diclofenac 75 mg 1–2 h preceding sexual activity [11]. Takeshima et al. administered 200 mg of celecoxib which proved effective in a single patient [3].

Immune system modulation has been proposed by some authors [6, 9, 16, 17, 19] with the beneficial effects of a hyposensitisation regimen being clearly demonstrated. This consists of multiple subcutaneous injection of autologous semen with gradually increasing concentration and decreasing frequency over three years. Reported success rates are between 60 to 90% with the additional benefit of an improvement in intravaginal ejaculatory latency time [6, 9, 17].

An alternative approach to immunotherapy is the use of monoclonal anti-IgE antibody omalizumab. This was administered at 300 mg at a 4-weekly interval [22].

In addition, there have been isolated individual reports of novel successful therapies including intralymphatic autologous sperm

injection [16], muscle relaxation [23], and surgery to remove the epididymis and ligate the vas deferens [24].

POIS has significant negative impact on the mental health and well-being of both patients and their partners. Coping mechanisms such as abstinence may have an adverse effect on their relationship. A recent online survey in men with self-reported symptoms indicate that up to 51% of men have sought medical treatment for such symptoms [13].

Future areas of research may include the exact sequencing of treatments and further elucidating exact mechanisms underlying the syndrome. This may also include developing a single diagnostic test to identify all cases of POIS without depending solely on subjective symptom criteria.

CONCLUSION

Although POIS is a rare condition, it is vital for urologists to have a good knowledge of its presentation to improve awareness, increase diagnosis and avoid the potential pitfall of misdiagnosis.

Whilst there are still a great number of unknowns in relation to the prognosis and treatment of POIS, management strategies do exist, and it is important for all clinicians potentially dealing with such issues to have a sound knowledge of the options available and likelihood of success.

DATA AVAILABILITY

Data from the research is available within the article and can be provided on request from the authors(BO, IP).

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AUTHOR CONTRIBUTIONS

BO involved in study conception and design, data collection, analysis and manuscript preparation. IP involved in study conception and design, data collection, analysis and manuscript preparation. VB involved in study conception and design, and manuscript preparation.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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